REMARKS

The present application is directed to a method of treating a human or animal suffering from the effects of infection with *Yersinia pestis*, comprising administering to the human or animal a therapeutically effective amount of a medicament comprising an antibody specific for *Y. pestis* F1-antigen or a binding fragment thereof, and an antibody specific for *Y. pestis* V-antigen or a binding fragment thereof. Claims 17-32 are pending. Claims 25-32 are withdrawn as directed to a non-elected invention. In this Amendment and Response to Non-Final Office Action ("Response"), applicants amend Claims 17 and 20-23 to correct informalities, typographical errors and punctuation. The amendments do not introduce any new matter.

Rejection of Claims under 35 U.S.C. § 103(a)

The Examiner rejects Claims 17-24 under 35 U.S.C. § 103(a) as unpatentable over Hill *et al.* (*Infec. Immun.* 65:4476-4482 (1997); "Hill") in view of Anderson *et al.* (*Am. J. Trop. Med. Hyg.* 56:471-473 (1997); "Anderson") and Casadevall (*Clin. Immunol.* 93:5-15 (1999); "Casadevall"). On page 5 of the Office Action, the Examiner states that, at the time of the invention, it would have been obvious to one of ordinary skill in the art to combine antibodies against *Y. pestis* F1-antigen with antibodies against *Y. pestis* V-antigen to use in a method of treating a subject with a *Y. pestis* infection. The Examiner states it would also have been obvious to use humanized antibodies to avoid the toxic effects of heterologous antibodies. Applicants respectfully traverse the rejection.

MPEP 2142 states: "To reach a proper determination under 35 U.S.C. §103, the examiner must step backward in time and into the shoes worn by the hypothetical 'person of ordinary skill in the art' when the invention was unknown and just before it was made. In view of all factual information, the examiner must then make a determination whether the claimed invention 'as a whole' would have been obvious at that time to that person." Applicants respectfully assert that the currently pending claims would not have been obvious to one of ordinary skill in the art in the field of the present application at its priority date. At that point in time, it would not have been obvious to one of ordinary skill in the art to use antibodies against *Y. pestis* therapeutically,

such as in a claimed method of treating a human or an animal suffering from effects of an existing *Y. pestis* infection.

In contrast to the claimed method, Hill and Anderson disclose using antibodies against *Y. pestis* to prevent an infection with *Y. pestis*. As discussed by the Examiner on page 4 of the Office Action, Hill and Anderson disclose administering antibodies against *Y. pestis* to animals prior to infecting them with *Y. pestis*. A combination of Hill or Anderson fails to teach or suggest administering anti-*Y. pestis* antibodies therapeutically in order to treat an existing *Y. pestis* infection.

Casadevall, which the Examiner cites for its disclosure of therapeutic use of antibodies for treatment of various diseases, fails to teach or suggest antibody therapies against *Y. pestis* infection. Absence of such teaching or suggestion in Casadevall is due to the fact that, before the invention of the claimed embodiments of applicants' methods, antibody therapies have not been proposed as a treatment for *Y. pestis* infection (plague). *See* present application, specification, p. 4, line 33, through p. 5, line 1.

Contrary to the assertions of the Examiner in the Office Action, it would not have been obvious to one of ordinary skill in the art in the field of the present application to combine the general discussion of antibody therapies in Casadevall with the preventive use of anti-*Y. pestis* antibodies in Hill and Anderson in order to arrive at an effective anti-plague therapy. While antibody therapies in general were known prior to the invention of the claimed embodiments of applicants' methods, the effectiveness of such therapies in each particular situation was known to be uncertain. For example, Casadevall discusses variable efficacies of antibody therapies as one of the problems of this therapeutic approach (see Casadevall, p. 5, first column, first paragraph).

This general view expressed in Casadevall is reinforced, for example, by Kriel and Eibl (*J. Virol.* 71:2921-2927 (1997); "Kriel," copy enclosed as Exhibit A). Kriel further supports applicants' position that, at the time of the invention of the embodiments of applicants' methods recited in the claims, one of ordinary skilled in the art in the field of the present application did not expect that a post-exposure treatment of an infectious disease with antibodies would

necessarily be effective. In particular, Kriel discloses that post-exposure therapy with immunoglobulin can, in fact, worsen the outcome of an infectious disease due to antibody-dependent enhancement. *See, for example,* Kriel, *Abstract.*

Thus, Kriel teaches away from the claims and disagrees with the Examiner's position that an antibody therapy of an infectious disease was expected to be effective or even desirable in every case. To the contrary, Casadevall and Kriel both show that, before the priority date of the present application, one of ordinary skill in the art in the area of infectious diseases knew that effectiveness antibody therapies was uncertain, and, even further, was aware of the very real possibility that treatment with antibodies may, in fact, have a negative effect on a patient. The teaching of Kriel regarding potentially deleterious effects of antibody therapies is not limited to the specific infections that the authors of the paper experimentally investigated. Kriel clearly acknowledges on page 2921, first paragraph, that "in the context of active and passive immunization strategies...ADE [antibody dependent enhancement] of infection is always a concern" (emphasis added).

Wahl *et al.* (*J. Hepatol.* 9:198-203 (1989); "Wahl", *Abstract* enclosed as Exhibit B) further supports applicants' view that, applicants' claims are unobvious in view of the publications cited by the Examiner at least because, at the time of the invention of the claimed embodiments, antibody therapies of infectious diseases, such as those recited in the claimed methods, were not expected to be necessarily effective. *See* Wahl, *Abstract.* Wahl demonstrates experimentally that anti-Hepatitis B antibodies administered post-exposure to the Hepatitis B virus failed to stop the development of Hepatitis B infection in primates, unless combined or co-administered with vaccination. Applicants therefore, assert that Casadevall, Kriel and Wahl all evidence that one of ordinary skill in the art in the field of the present application would not have found the claimed methods obvious.

In order to support a rejection under 35 U.S.C. 103, the Examiner appears to use "obvious to try" rationale. *See* MPEP 2141(III); 2143(E). To reject a claim based on this rationale, the Examiner, first, must resolve the *Graham* factual inquires, namely, (a) determining the scope and content of the prior art, (b) ascertaining the differences between the claimed

invention and the prior art, and (c) resolving the level of ordinary skill in the pertinent art. *See* MPEP 2141(II) citing *Graham v. John Deere Co.*, 383 U.S. 1 (1966); MPEP 2143(E). Applicants assert that, when determining the scope and content of prior art, the Examiner failed to take into account that, although Casadevall's antibody therapies in general, along with some specific examples of their use for the treatment of infectious diseases, such as pneumococcal pneumonia on page 5, Casadevall fails to teach or suggest using such therapies as an effective treatment of *Y. pestis* infection. Furthermore, Casadevall discloses that variable efficacies of antibody therapies as one of their known problems.

After resolving *Graham* factual inquires, the Examiner should articulate several findings, including a finding that "one of ordinary skill in the art could have pursued the known potential solution with a reasonable expectation of success." Applicants assert such a finding is unjustified based on combined teachings of Hill, Anderson and Casadevall. In particular, Applicants assert that, based on the disclosure of Casadevall regarding problems associated with antibody therapies, one of ordinary skill in the art in the field of the present application would not have had a reasonable expectation that antibodies disclosed in Hill an Anderson for prevention of *Y. pestis* infection would also be effective in the treatment of *Y. pestis* infection. Applicants further assert that the additional evidence provided with this response, namely, Kriel and Wahl, shows that, at the time applicants' invented the claimed embodiments of their methods, one of ordinary skill in the art did not have a reasonable expectation of success of the claimed methods.

Furthermore, applicants discovered that a combination of antibody specific for *Y. pestis* F1-antigen and an antibody specific for *Y. pestis* V-antigen acts synergistically when used in treatment of an existing *Y. pestis* infection. *See*, for example, the specification of the present application, page 4, lines 1-5, page 16, lines 2-5. The synergistic effect of the combined antigens is further demonstrated by additional data provided in a peer-reviewed publication of applicants' further research in the area of the present application, namely, Hill *et al*, *Infect. Immun.* 71:2234-2238 (2003);"Hill 2003," a copy enclosed as Exhibit C). Figure 2 of Hill 2003, provided on p. 2237 of the publication, clearly shows that the combined effect of the F1-antigen and V-

antigen specific antibodies, when administered 48 hours post infection, is more than additive, when compared with administration of the individual antibodies alone. This additional unexpected finding further supports applicants' position that the claimed method, as a whole, would not have been obvious at the priority date of the present application to a person of ordinary skill in the art.

In view of the foregoing, applicants respectfully assert that a combination of Hill, Anderson and Casadevall fails to render obvious currently pending claims. Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 103(a).

CONCLUSION

The foregoing is submitted as a complete Response to the Notice of Non-Compliant Amendment mailed August 11, 2008. Applicants submit that the claims in the present application are in condition for allowance, and such action is courteously solicited. No additional fees are believed due; however, the Commissioner is hereby authorized to charge any deficiency, or credit any overpayment, to Deposit Account No. 11-0855.

If the Examiner believes that any informalities remain in the case, which may be corrected by Examiner's amendment, or that there are any other issues which can be resolved by a telephone interview, a telephone call to the undersigned agent at (404) 815-6102 is respectfully solicited.

Respectfully submitted,

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